Impact of hypertension on infarct size in ST elevation myocardial infarction patients undergoing primary angioplasty.

Original Article

Impact of hypertension on infarct size in ST elevation myocardial infarction patients undergoing primary angioplasty

Giuseppe De Luca[a], Guido Parodi[b], Roberto Sciagrà[c], Benedetta Bellandi[b], Vincenzo Comito[b], Ruben Vergara[b], Angela Migliorini[b], Renato Valenti[b], and David Antoniucci[b]

Background: Hypertension is a well known risk factor for atherosclerosis. However, data on the impact of hypertension in patients with ST-segment elevation myocardial infarction (STEMI) are inconsistent, and mainly related to studies performed in the thrombolytic era, with very few data on patients undergoing primary angioplasty. The aim of the current study was to evaluate the impact of hypertension on scintigraphic infarct size in STEMI patients undergoing primary percutaneous coronary intervention (PCI).

Method: Our population is represented by 830 STEMI patients undergoing primary PCI. Infarct size was evaluated at 30 days by technetium-99m-sestamibi.

Results: Hypertension was associated with more advanced age ($P < 0.001$), a larger prevalence of diabetes ($P = 0.001$), female sex ($P < 0.001$), but lower prevalence of smoking ($P < 0.001$) and anterior infarction ($P = 0.042$). No difference was observed in ischemia time, cardiogenic shock at presentation, in preprocedural thrombolysis in myocardial infarction (TIMI) flow, and collateral circulation. Hypertension did not affect the rate of postprocedural TIMI 3 flow. Hypertension did not affect infarct size [12.5% (4.1–23.8%) vs. 12.8% (4.3–24.7%), $P = 0.38$]. Similar results were observed in subanalyses in major high-risk subgroups. No impact of hypertension on infarct size was confirmed when the analysis was conducted according to the percentage of patients with infarct size above the median [adjusted odds ratio (95% CI) = 0.97 (0.72–1.33), $P = 0.92$].

Conclusion: This study shows that among STEMI patients, undergoing primary PCI hypertension does not affect scintigraphic infarct size.

Keywords: hypertension, infarct size, percutaneous coronary intervention, primary angioplasty, ST elevation myocardial infarction

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; LV, left ventricle; SPECT, single-photon emission computer tomography; STEMI, ST-segment elevation acute myocardial infarction; TIMI, thrombolysis in myocardial infarction

INTRODUCTION

Availability of pharmacologic and mechanical reperfusion therapies has significantly reduced cardiac mortality among ST-segment elevation acute myocardial infarction (STEMI) patients [1–6]. However, even though primary angioplasty has been shown to provide larger benefits as compared with thrombolysis, a suboptimal myocardial reperfusion is observed in a still relevant proportion of patients, despite optimal epicardial recanalization [7–9]. Hypertension is an established risk factor for atherosclerosis [10]. However, data on the prognostic impact of hypertension in patients with STEMI are so far inconsistent, mainly related to studies performed in the thrombolytic era [11–15]. In fact, although elevated levels of heart failure, stroke, cranial hemorrhage, and mortality risk have been shown in patients with antecedent hypertension receiving thrombolytic therapy [10–16], still controversial is the prognostic role of hypertension in terms of survival after primary angioplasty [17–20]. In particular, few data focused on the impact of hypertension on infarct size. Therefore, the aim of the current study was to evaluate the impact of hypertension on scintigraphic infarct size in STEMI patients undergoing primary angioplasty.

MATERIALS AND METHODS

Our initial population included 894 patients with STEMI treated by primary angioplasty scheduled to undergo evaluation of the infarct size at 30 days after the intervention [21]. A total of 64 patients [16 women (8.7%) and 48 men (7.4%)] were excluded because of death ($n = 16$), reinfarction ($n = 7$), or target vessel revascularization ($n = 11$) within 30 days from revascularization, or refusal to undergo

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[a]Division of Cardiology, 'Maggiore della Carità' Hospital, Eastern Piedmont University, Novara, [b]Division of Cardiology, Careggi Hospital and [c]Nuclear Medicine Unit, University of Florence, Florence, Italy

Correspondence to Giuseppe De Luca, MD, PhD, Division of Cardiology, 'Maggiore della Carità' Hospital, Eastern Piedmont University, Novara, Italy. Tel: +39 0321 3733141; fax: +39 0321 3733407; e-mail: giuseppe.deluca@maggioreosp.novara.it

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scintigraphy ($n = 30$). Therefore, our final population was 830 patients. All patients were admitted within 12 h from symptom onset, and received at the time of diagnosis aspirin (500 mg intravenously), heparin (60 IU/kg intravenously), β-blockers, and nitroglycerine intravenously if not contraindicated, but the decision to provide glycoprotein IIb-IIIa inhibitors was left to the discretion of the operator at the time of intervention. All patients were on dual oral antiplatelet therapy (aspirin and clopidogrel or ticlopidine) for at least 4 weeks after stent implantation. All demographic, clinical, procedural, and in-hospital and follow-up data were collected in a database. Patients were categorized as having antecedent hypertension, if this diagnosis was known by the patient to have been made by the family physician or after specialist referral and/or the admission note indicated a history of hypertension.

Coronary angiography and mechanical revascularization

Selective coronary angiography was performed in multiple projections before mechanical reperfusion. Immediately after diagnostic angiography, percutaneous coronary intervention (PCI) with stenting of the infarct-related vessel was performed using standard material. Successful primary PCI was defined as thrombolysis in myocardial infarction (TIMI) grade 3 coronary flow in the treated vessel with a residual stenosis less than 20%.

Infarct size assessment

As previously described [21], gated single-photon emission computed tomography (SPECT) acquisition began 60 min after technetium-99m-sestamibi injection (740 MBq), using a double-head gamma-camera equipped with high-resolution collimators, 180° rotation arc, 32 projections, 60 s/projection, 8 frames/heart cycle, and 64×64 matrices. The studies were reconstructed using filtered back-projection without attenuation or scatter correction and realigned along the heart axis. Perfusion defects were quantified as percentage involvement of left ventricular wall, with the defect threshold set at 60% of peak uptake [22].

Statistical analysis

Statistical analysis was performed using the SPSS, version 15.0, statistical package (SPSS, Chicago, Illinois, USA). Continuous data are expressed as the median (25th–75th percentiles) and categorical data as percentages. The analysis of variance test or Mann–Whitney *U*-test was appropriately used for continuous variables, according to the normality of distribution, as evaluated by the Shapiro–Wilk test. The χ^2 test or Fisher's exact test was used for categorical variables. Multiple logistic regression analysis was used to evaluate the effect of hypertension on infarct size (as above the median) after adjustment for significant ($P < 0.05$) confounding baseline characteristics. Interaction between hypertension and other major variables (age, sex, diabetes, infarct location, ischemia time) on infarct size was evaluated by analyzing the categorical by continuous variable interactions, as previously described [23].

RESULTS

Patients' characteristics are shown in Tables 1 and 2. Hypertension was associated with more advanced age ($P < 0.001$), a larger prevalence of diabetes ($P = 0.001$), female sex ($P < 0.001$), but lower prevalence of smoking ($P < 0.001$) and anterior infarction ($P = 0.042$). As expected, hypertension was associated with higher SBP ($P = 0.045$) and DBP ($P = 0.011$) at admission, without any difference in heart rate. No difference was observed in ischemia time, cardiogenic shock at presentation, in preprocedural TIMI flow, and collateral circulation. Hypertension did not affect the rate of postprocedural TIMI 3 flow.

As shown in Figure 1, hypertension did not affect infarct size [12.2 (4.1–23.8) vs. 12.8 (4.3–24.7), $P = 0.38$]. Similar results were observed in subanalyses according to advanced age [<65 years: 12.5% (4.55–21.7%) vs. 12.8% (5–24.4%), $P = 0.25$; >65 years: 12.1% (3.4–24.8%) vs.

TABLE 1. Demographic and clinical characteristics according to history of hypertension

Variable	Hypertension ($n = 362$)	Control ($n = 468$)	*P* value
Age	67 (59–75)	61 (53–69)	<0.001
Age >75 years (%)	26.8	15	<0.001
Female sex (%)	28.7	14.7	<0.001
Smoking (%)	37.3	56.8	<0.001
Dyslipidemia (%)	35.1	33.1	0.55
Diabetes (%)	18.2	10.5	0.001
Previous MI (%)	4.7	3.6	0.44
Previous CABG (%)	0.6	1.1	0.42
Previous PTCA (%)	4.2	3.2	0.52
Ischemia time (min)	204 (145–272)	200 (149–275)	0.42
Ischemia time >3 h (%)	59.9	58.8	0.75
Anterior MI (%)	36.2	43.2	0.042
[a]Cardiogenic shock (%)	4.1	3.8	0.83
[a]SBP (mmHg)	125 (110–140)	120 (105–140)	0.045
[a]DBP (mmHg)	80 (70–85)	70 (65–80)	0.011
[a]Heart rate (bpm)	72 (60–81)	74 (65–81)	0.35

CABG, coronary artery bypass grafting; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.
[a]At hospital admission.

TABLE 2. Angiographic and procedural characteristics according to history of hypertension

Variable	Hypertension ($n=362$)	Control ($n=468$)	P value
Collateral circulation			0.31
RENTROP 0 (%)	92.3	87	
RENTROP 1 (%)	5.4	8.5	
RENTROP 2 (%)	2.4	3.6	
RENTROP 3 (%)	0	0.8	
Preprocedural TIMI flow			0.43
TIMI 0–1 (%)	80.6	81.8	
TIMI 2 (%)	10	11.2	
TIMI 3 (%	9.4	7.1	0.22
Infarct-related artery			0.21
RCA (%)	48.6	42.7	
Cx (%)	15.2	13.7	
Graft (%)	0	0.2	
LAD (%)	36.2	43.2	
LM (%)	0	0.2	
Multivessel disease (%)	43.9	39.6	0.22
Number of lesions			0.28
1 (%)	72.9	78.4	
2 (%)	21.3	16.5	
3 (%)	5.8	5.2	
Abciximab (%)	88.9	91.4	0.22
Stenting (%)	100	98	0.95
IABP (%)	3.6	3.8	0.85
Postprocedural TIMI 3 flow (%)	93.3	91.4	0.33

Cx, circumflex; IABP, intraaortic balloon pump; LAD, left anterior descending; LM, left main; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

13.3% (4–25.1%), $P=0.78$; P interaction $=0.74$], sex [female sex: 5.25% (0–17.8%) vs. 8.6% (0–21.5%), $P=0.23$; male sex: 14% (6.3–25.1%) vs. 13.9% (5.5–25.9%), $P=0.65$; P interaction $=0.38$], diabetes [diabetic patients: 10.3% (3.3–25%) vs. 10% (4–23.6%), $P=0.96$; no diabetes: 12.5% (4.5–23.8%) vs. 13.7% (4.6–24.8%), $P=0.28$; P interaction $=0.52$], ischemia time [<3 h: 9.6% (4.5–17.8%) vs. 11.6% (4–22.1%), $P=0.13$; >3 h: 15.1% (4–25.2%) vs. 15% (5.1–26.5%), $P=0.89$; P interaction $=0.19$], and infarct location [anterior STEMI: 15.5% (6.1–29.1%) vs. 16% (5.6–29.7%), $P=0.97$; nonanterior STEMI: 10.7% (2–21%) vs. 11.8% (3.9–21.5%), $P=0.39$; P interaction $=0.64$]. No relationship was observed between SBP ($r=0.06$, $P=0.25$), DBP ($r=0.04$, $P=0.42$) at admission with infarct size.

Similar results were observed when the analysis was conducted according to the percentage of patients with infarct size above the median (Figure 2), which were confirmed after correction for baseline characteristics, such as age, smoking, diabetes, sex, anterior MI, and blood pressure at admission [odds ratio, OR (95% confidence interval, CI) = 0.97 (0.72–1.33), $P=0.92$].

DISCUSSION

This is one of the largest studies so far conducted showing no impact of hypertension on scintigraphic infarct size in STEMI patients undergoing primary PCI.

Hypertension currently represents a major risk factor for atherosclerosis and heart failure. However, still controversial is its prognostic impact after STEMI. Several mechanisms may contribute to explain a potential impact of hypertension on outcome after STEMI. Patients with hypertension may have higher risk profile, such as more advanced age, higher rates of diabetes, and more extensive coronary artery disease (CAD; 10–20). However, higher diastolic pressure may improve collateral circulation and coronary perfusion and may, therefore, positively impact on the success of reperfusion and infarct size. In addition, a thicker left ventricle may positively affect left ventricular remodeling, with a reduction in left ventricular dilatation [19].

Several reports have investigated the prognostic impact of hypertension on outcome among patients treated with thrombolysis. Rabkin *et al.* [11] showed a negative impact of hypertension on short-term and long-term outcome in STEMI patients. In the Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto (GISSI-2) study, in-hospital and 6-month mortality in hypertensive STEMI patients were significantly higher compared with normotensive individuals [12], as was the rate of left ventricular failure, recurrent angina, and recurrent MI. Aylward *et al.* [13], evaluating all

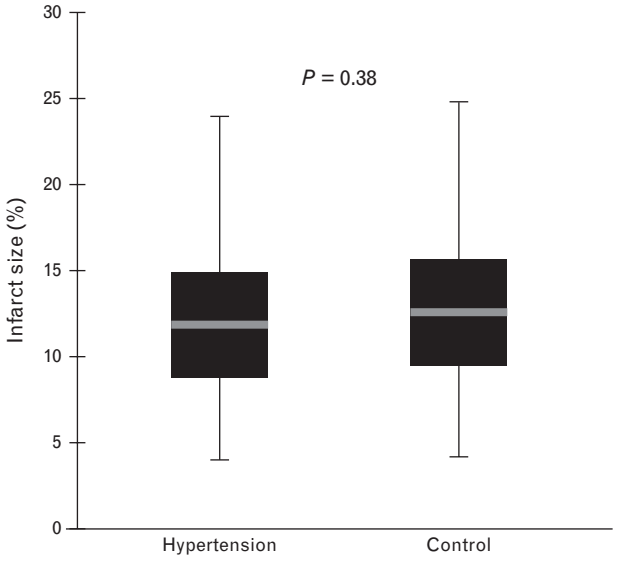

FIGURE 1 Bar graphs show the impact of hypertension on infarct size. Data are presented as median (25th–75th percentile).

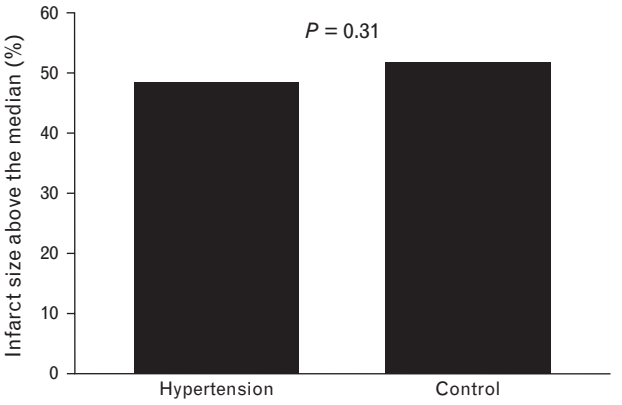

FIGURE 2 Bar graphs show the impact of hypertension on infarct size (as percentage of patients above the median).

patients participating in the GUSTO-1 study, observed that the risk of an early death was higher in patients with elevated SBP. In a study by Majahalme *et al.* [14], in-hospital and 6-month mortality in hypertensive and normotensive acute coronary syndrome (ACS) patients were similar, whereas the rate of recurrent angina, paroxysmal atrial fibrillation, and acute renal failure was higher among patients with hypertension.

While the negative prognostic impact of hypertension after thrombolysis in patients STEMI, has been clearly demonstrated, and mainly due to higher rates of heart failure, stroke, cranial hemorrhage, and mortality [10–16], only a few studies [17–20] have assessed the impact of hypertension on outcome after primary angioplasty, which currently represents the best reperfusion strategy.

Abrignani *et al.* [18] observed that hypertensive patients with first acute myocardial infarction (AMI) have a better in-hospital outcome than age-matched and sex-matched normotensive individuals. On the contrary, in a recent paper by Rembek *et al.* [17] performed in 366 STEMI patients submitted to mechanical revascularization, no difference was observed in in-hospital mortality between hypertensive and normotensive patients. Parodi *et al.* [19] analyzed the impact of hypertension on 6-month left ventricular remodeling and 5-year outcome in 953 STEMI patients undergoing primary angioplasty, showing no impact on remodeling and mortality. However, hypertension was associated with higher risk of heart failure due to diastolic dysfunction.

In a recent study, Lazzeri *et al.* [20] in a population of 560 STEMI patients without known diabetes, showed at a median follow-up of 32 months no impact of hypertension on mortality.

This is the first study investigating the impact of hypertension on infarct size as evaluated by scintigraphic technique. In accordance with previous studies, we found that patients with hypertension have a higher risk profile, being older, with higher prevalence of female sex, diabetes, but lower prevalence of smoking and anterior MI. No difference was observed in preprocedural TIMI flow, extension of CAD, and coronary collaterals. In particular, no difference was observed in postprocedural TIMI 3 flow. Hypertension was not associated with larger infarct size, even after correction for baseline confounding factors and in major high-risk subgroups of patients.

Study limitations

We assessed infarct size 1 month after the index infarction instead of at hospital discharge, as in the majority of previously published studies. On the other hand, this circumstance should be more effective in preventing interference of myocardial stunning with the extent of perfusion defects [24]. Coronary angiographic control before gated SPECT to allow the exclusion of infarct-related vessel restenosis was not routinely performed. Caution should be exercised in extending our conclusions to all STEMI populations. In fact, our patients were part of randomized trials that had scintigraphic infarct size as an endpoint. Therefore, patients included in our study were, by definition, survivors at 30 days, with a subsequent potential selection bias. Uncontrolled hypertension during the course of infarction, as much as at the time of scintigraphy, might have influenced infarct size evaluation. Unfortunately, with the only exception of blood pressure values at admission, which were not associated with infarct size, detailed data on blood pressure control were not available. Furthermore, the definition of hypertension was based on clinical history at admission. While this may certainly represent a limitation, it must be recognized that the use of blood pressure at admission may be misleading, because it may be influenced by the infarction and the associated psychological stress, and therefore may not certainly be a marker of hypertension. Finally, data on weight/BMI were not collected and, therefore, unavailable.

In conclusion, this study showed that among STEMI patients, undergoing primary angioplasty hypertension does not affect scintigraphic infarct size.

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Conflicts of interest

There are no conflicts of interest.

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Reviewers' Summary Evaluations

Reviewer 1

The strength of this study lies in the large number of study participants and the measurement of infarct size representing a new approach to this still debated topic. A weakness of the study is that the measurement of infarct size was made 30 days after PCI, which could have biased the results towards less severe cases. Another weakness is some lack of information on the severity of hypertension.

Reviewer 2

This observational study examines the influence of a prior history of hypertension on scintigraphic measures of infarct size in 30 day survivors of acute MI after initial PCI treatment. The investigators found no influence of a history of HT on scintigraphic infarct size. This is somewhat surprising since the massively larger GISSI-2 & GUSTO-1 trials of thrombolysis had found an influence of prior HT. The reason for the different results after PCI is unclear.